37

UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/089,525	10/07/2002	Jamey D Marth	19452A-6-1US	9242

20350 7590 03/06/2006

TOWNSEND AND TOWNSEND AND CREW, LLP
TWO EMBARCADERO CENTER
EIGHTH FLOOR
SAN FRANCISCO, CA 94111-3834

EXAMINER	
ZARA, JANE J	

ART UNIT	PAPER NUMBER
1635	

DATE MAILED: 03/06/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/089,525	MARTH ET AL.	
	Examiner	Art Unit	
	Jane Zara	1635	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *11 January 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,6,7,10-12,30 and 37-40* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,6,7,10-12,30,37-40* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

This Office action is in response to the communication filed 1-11-06.

Claims 1, 6, 7, 10-12, 29, 30 and 37-40 are pending in the instant application.

Continued Examination Under 37 CFR 1.114

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 1-11-06 has been entered.

Response to Arguments and Amendments

Withdrawn Rejections

Any rejections not repeated in this Office action are hereby withdrawn.

Maintained Rejections/Rejections Necessitated by Amendments

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1, 6, 7, 10-12, 29, 30 and 37-40 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s)

contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention for the reasons of record set forth in the Office actions mailed 2-10-05 and 9-7-05 and for the reasons of record set forth below.

The claims are drawn to compositions and methods for modulating levels of vWF or FVIII in an animal comprising the administration of any ST3Gal-IV substrate analog which effectively inhibits ST3Gal-IV sialyltransferase activity, and which method of modulation is performed in conjunction with administration of a drug for which blood clotting is a potential side effect.

The specification and claims do not adequately describe the broad genus comprising *ST3Gal-IV substrate analogs* which effectively inhibit ST3Gal-IV sialyltransferase activity in an animal and provide for the treatment effects claimed. The specification and claims do not adequately describe the broad genus comprising *a drug for which blood clotting is a potential side effect*, and for which co-administration of any species of ST3Gal-IV substrate analogs would provide for the treatment effects presently claimed . The specification and the art provide mention of ST3Gal-IV substrate analogs which have been identified as inhibitors of ST3Gal-IV sialyltransferase activity in vitro, and which include CMP-sialic acid analogs and transition state analogs. But the art and the instant disclosure are silent regarding the ability to utilize a representative number of species of this genus in vivo, whereby treatment effects are provided upon administration of any analog, or whereby treatment

effects are provided upon co-administration of these analogs with any drug for which blood clotting is a potential side effect. The recitation of in vitro studies involving the identification and/or characterization of various inhibitors within the genus claimed does not satisfy the written description requirement because it is unclear which of these analogs would provide the treatment effects claimed in an animal, either alone or upon co-administration with any drug for which blood clotting is a potential side effect.

Applicant's arguments filed 1-11-06 have been fully considered but they are not persuasive. Applicant argues that in vivo success has been observed in using glycosyltransferase inhibitors such as tunicamycin for treating viral or bacterial infections and that tunicamycin can cross the cell membrane but still readily binds to the active site of the enzyme. Applicant is correct that tunicamycin has been used successfully in vivo to treat various infections, but it is unclear how an example of this inhibitor of N-acetyl glucosaminyl transferases in inhibiting viral or bacterial infections in vivo is representative of the genus claimed, which genus is drawn to *ST3Gal-IV substrate analogs* which effectively inhibit ST3Gal-IV sialyltransferase activity in an animal and provide for the treatment effects claimed.

The specification provides no guidance of what structural features are common to the viral/bacterial inhibitors mentioned in Applicant's arguments (*i.e.* 2-deoxy-D-glucose or tunicamycin) and the broad genus claimed (*i.e.* ST3Gal-IV substrate analogs which effectively inhibit ST3Gal-IV sialyltransferase activity in an animal and provide for the treatment effects claimed, alone or in combination with the administration of any drug for which blood clotting is a potential side effect). Since the specification does not

adequately describe the analogs required to practice the methods claimed, it does not adequately describe the claimed methods or compositions.

Claims 1, 6, 7, 10-12, 29, 30 and 37-40 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for the in vitro inhibition of ST3Gal-IV sialyltransferase activity upon administration of ST3Gal-IV substrate analogs, does not reasonably provide enablement for in vivo inhibition or treatment effects for the reasons of record set forth in the Office actions mailed 2-10-05 and 9-7-05 and for the reasons of record set forth below.

The claims are drawn to compositions and methods for modulating levels of vWF or FVIII in an animal comprising the administration of any ST3Gal-IV substrate analog which effectively inhibits ST3Gal-IV sialyltransferase activity, and which method of modulation is performed in conjunction with administration of a drug for which blood clotting is a potential side effect.

Applicant's arguments filed 1-11-06 have been fully considered but they are not persuasive. Applicant argues that the biochemistry pertinent for glycosyltransferase activity was well understood at the time the invention was made and that the approaches are generally applicable to different glycosyltransferases, including sialyltransferases. Applicant argues that in vivo success has been observed in using glycosyltransferase inhibitors such as tunicamycin for treating viral or bacterial infections and that tunicamycin can cross the cell membrane but still readily binds to the active site of the enzyme. Applicant is correct that tunicamycin has been used

successfully in vivo to treat various infections, but it is unclear how an example of this inhibitor of N-acetyl glucosaminyl transferases in inhibiting viral or bacterial infections in vivo is representative or enabling of the genus presently claimed, which genus is drawn to ST3Gal-IV substrate analogs which effectively inhibit ST3Gal-IV sialyltransferase activity in an animal and which provide for the treatment effects claimed. Contrary to Applicant's assertions, the administration of inhibitors of upstream transferases, such as tunicamycin to inhibit bacterial or viral infections in an organism, is not representative or correlative of the ability to inhibit ST3Gal-IV sialyltransferase activity in a mammalian target cell in an organism. Furthermore, Applicant admits that it is unclear which sialyltransferase is responsible for the transfer of the terminal vWF sialic acids (see p. 3 of the instant specification, PCT/US00/26550).

The uncertainty/unpredictability of the instantly claimed invention lies not in the biochemical characterization of the substrate analogs in their ability to inhibit a target enzyme, it lies instead in the undue experimentation required to deliver adequate amounts of known ST3Gal-IV substrate analogs to the proper target cells (and appropriate subcellular organelles) harboring the ST3Gal-IV sialyltransferase (or other sialyltransferase responsible for sialylating the vWF). The instant specification teaches the ablation of ST3Gal-IV in mice and corresponding effects on glycosylation and in the amount of vWF in mice. The phenotypes observed upon ablation of ST3Gal-IV sialyltransferase in mice is not representative or correlative of the ability to effectively deliver ST3Gal-IV substrate analogs to an organism, whereby ST3Gal-IV sialyltransferase is inhibited and treatment effects are provided.

The ability to provide antibiotic effects (*e.g.* providing toxic effects to bacterial cells, as asserted by Applicant) using glycosyltransferase analogs is not representative or correlative of the ability to provide treatment effects in vivo upon administration of substrate analogs to mammalian target cells. The concentration requirements and delivery issues involving mammalian target cells (and the requisite subcellular organelles) are different than those involving target bacterial cells. In addition, the inhibition of one glycosyl transferase using one inhibitor is not necessarily predictive or correlative of the ability to inhibit a different target enzyme using a different inhibitor. In vivo treatment comprising administration of the various members of the instantly claimed genus requires undue experimentation beyond that taught in the instant disclosure, and beyond that taught in the art. For these reasons, the instant rejection for lacking enablement is maintained.

New Rejections

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1, 6, 7, 10-12, 29, 30 and 37-40 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The metes and bounds of "modulating" levels of vWF or FVIII cannot be determined (e.g. The term *modulating* embraces both increasing and decreasing levels

of vWF or FVIII. It is unclear how inhibiting ST3Gal-IV sialyltransferase will lead to an increase and a decrease in vWF or FVIII.). Appropriate clarification is requested.

Conclusion

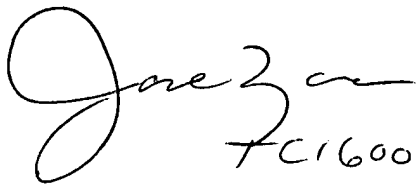
Certain papers related to this application may be submitted to Art Unit 1635 by facsimile transmission. The faxing of such papers must conform with the notices published in the Official Gazette, 1156 OG 61 (November 16, 1993) and 1157 OG 94 (December 28, 1993) (see 37 C.F.R. 1.6(d)). The official fax telephone number for the Group is **571-273-8300**. NOTE: If Applicant *does* submit a paper by fax, the original signed copy should be retained by applicant or applicant's representative. NO DUPLICATE COPIES SHOULD BE SUBMITTED so as to avoid the processing of duplicate papers in the Office.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to **Jane Zara** whose telephone number is **(571) 272-0765.** If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Andrew Wang, can be reached on (571) 272-0811. Any inquiry regarding this application should be directed to the patent analyst, Katrina Turner, whose telephone number is (571) 272-0564. Any inquiry of a general nature or relating to the status of this application should be directed to the Group receptionist whose telephone number is (703) 308-0196.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for

published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Jane Zara
3-1-06



JANE ZARA, PH.D.
PRIMARY EXAMINER